UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,316	08/22/2001	Ching-Leou Teng	ISIS-4824	1463

34138 7590 07/01/2004

COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,316	TENG ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ ~~Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)~~ Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 5/3/04. The amendment has been entered. Claims 1-15 have been cancelled. Claims 16-27 are currently pending in the application and are examined herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 16-18 and 20-24 remain rejected and claims 26 and 27 are now rejected (in view of the amendment) under 35 U.S.C. 102(b) as being anticipated by US Patent 5,877,309 (McKay et al.), for the reasons of record, which are reiterated below for convenience.

3. The instant claims are drawn to:

A method for enhancing the intestinal absorption of a drug in an animal, comprising orally administering to said animal an oral formulation. comprising:

(a) a first population of carrier particles comprising said drug and a bioadhesive compound; and

(b) a second population of carrier particles comprising a penetration enhancer (claim 16); wherein the animal can be a mammal (claim 17) or a human (claim 18); wherein the carrier particles are administered together (claim 20); wherein the drug is an oligonucleotide (claims 21); wherein the penetration enhancer is the fatty acid capric acid (claim 22); wherein the bioadhesive is a polyacrylic polymer (claim 23); and wherein the oligonucleotide is an antisense oligonucleotide (claim 24). Claims 26 and 27 have been amended such that they encompass the method of claim 23 wherein the bioadhesive comprises a polyacrylic polymer (claim 26), wherein the bioadhesive further comprises a hydroxypropylmethylcellulose (HPMC) (claim 27).

As previously indicated, McKay teaches a method which comprises administering to a human a composition comprising an antisense oligonucleotides as a drug, wherein the antisense oligonucleotide is comprised in a formulation which can comprise capric acid and polyacrylates (e.g., see: col. 20, lines 52-54, column 6, lines 29-65; col.22, lines 4-19; col. 23, lines 24-40; col. 25, lines 1-7; and col. 28, lines 3-4). Furthermore, McKay teaches that the antisense drug composition can comprise hydroxypropylmethylcellulose and polyacrylates (e.g., see col. 23, lines 29-40).

Response to Arguments

Applicant's arguments filed 5/4/04 have been fully considered but they are not persuasive. Applicants argue that the claims require a first population of carrier particles comprising said drug and a bioadhesive compound and a second population of particles comprising a penetration enhancer (see p. 5 of the response). Applicants acknowledge that the McKay patent teaches a composition comprising polyacrylate and capric acid, but Applicants argue that the reference does not teach that the polyacrylate is part of a first population of carrier

particles or that the capric acid is part of a second population of carrier particles, and therefore, applicants assert, the reference does not anticipate the claimed invention.

In response, a careful analysis of the claims reveals that claim 16 is drawn to:

A method for enhancing the intestinal absorption of a drug in an animal, comprising orally administering to said animal an oral formulation. comprising:

(a) a first population of carrier particles comprising said drug and a bioadhesive compound; and

(b) a second population of carrier particles comprising a penetration enhancer.

Dependent claim 19 requires that the first and second population of carriers are administered in a separately, while claim 20 (which also depends of claim 16) requires that the first and second population of carrier particles are administered in a single dosage form. Therefore, claim 16 must encompass the drug composition wherein the carrier particles are administered in a single dosage form, as well as in separate dosages. To the extent that the instant claims encompass administering a single dosage form (which is described in the specification as the "preferred embodiment") the rejection is considered appropriate because the claim clearly encompasses a single dosage form of a composition comprising capric acid and polyacrylate and/or HPMC. As such, there is no limitation that the first and second population of carrier particles are separate, as appears to be the Applicants argument. To the extent that the single dosage form comprises the two populations of carrier particles, there is no indication that the two populations are separated in any way in the single dosage. As such, the composition taught by McKay appears to be identical in structure and function to the claimed composition. Therefore, to the extent that they read on a single dosage form of the composition, anticipate the

instant claims. It is acknowledged that McKay does not explicitly teach that the first and second populations of carrier particles are administered separately. Therefore, the rejection of claim 19 under 32 USC 102 is withdrawn.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 16, 21 and 25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.), further in view of US Patent 5,514,788 (Bennett et al.), for the reasons of record which are reiterated below for convenience.

It is noted that McKay teaches a method for enhancing the intestinal absorption of a drug in an animal, comprising orally administering to said animal an oral formulation comprising: (a) a first population of carrier particles comprising said drug and a bioadhesive compound; and (b) a second population of carrier particles comprising a penetration enhancer (claim 16); wherein the drug is an oligonucleotide (claims 21), and specifically where the drug is an antisense oligonucleotide, as previously indicated.

McKay does not teach that the oligonucleotide has SEQ ID NO: 1 (claim 24).

However, Bennett teaches an antisense oligonucleotide that exactly matches SEQ ID NO: 1 of the instant claims (see SEQ ID NO: 22 in column 35 of Bennett) wherein the antisense oligonucleotide is contemplated for use in a method where it is administered to an animal (e.g., see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by McKay such that the antisense oligonucleotide described by Bennett (which is SEQ ID NO: 1) was the oligonucleotide drug used in the method, with a reasonable expectation of success.

The motivation to make the modification is provide in part by both McKay and Bennett. Specifically, McKay teaches a method for orally administering any therapeutic oligonucleotide to an animal and Bennett teaches a specific antisense oligonucleotide (that has SEQ ID NO: 1) is a therapeutic antisense oligonucleotide that can be administered to animals.

Response to Arguments

Applicant's arguments filed 5/4/04 have been fully considered but they are not persuasive. Similar to the arguments against the rejection of claims under 35 USC 102, Applicants argue that the instant claims are drawn to a method wherein the method encompasses administering a first population of carrier particles and a second population of carrier particles. Applicants assert that the cited reference does not teach a first and second population of carrier particles and therefore the reference is not applicable to the instant rejection. In response, as indicated above, the claims encompass administration of the first and second population of particles to a subject wherein the two populations of particles are administered in a single dosage form (which is described as the "preferred embodiement"). The cited reference teaches a method wherein a composition comprising all elements of claims are administered to a subject in a single dosage form. To the extent that the instant claims encompass administering a single dosage form (which is described in the specification as the "preferred embodiment") the rejection is considered appropriate because the claim clearly encompasses a single dosage form of a

composition comprising the claimed elements. As such, there is no limitation that the first and second population of carrier particles are separate, as appears to be the Applicants argument. To the extent that the single dosage form comprises the two populations of carrier particles, there is no indication that the two populations are separated in any way in the single dosage form. Therefore, the McKay reference is considered appropriate and the is applicable in the instant 103 rejection. Therefore the rejection is not withdrawn.

New Rejection
Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.).

It is noted that the claims encompass a method wherein a first population of particles (bioadhesive) and a second population of particles (penetration enhancer) are administered to a subject. Claim 16 is broad and can encompass administering the two populations of carrier

particles in a single dosage form or separately. Claim 19 explicitly indicates that the two populations of carrier particles are administered separately. To the extent that the instant claims are drawn to administering the two populations of carrier particles separately, the instant rejection is appropriate. McKay teaches a method for enchancing the intestinal absorption of a drug comprising administering a bioadhesive (such as a polyacrylate) and a penetration enhancer (such as capric acid) wherein the bioadhesive and penetration enhancer are administered separately. Although McKay does not explicitly teach that the bioadhesive particles and penetration enhancer particles are administere separately, it is noted that it was know in the prior art (based on the disclosure in the specification) that:

"While their specific mechanism of action is unknown, penetration enhancers are known to make the [GI] mucosal membrane more permeable to co- or subsequently administered drugs. Indeed, studies have shown that such drugs may be administered to up to one hour after the instillation of selected penetration enhancers with almost equivalent uptake." (see p. 2 of the specification (lines 4-8).

As such, it was well known in the art that the penetration enhancer and the bioadhesive particles can be administered separately, up to one hour apart and still deliver the drug to the cells.

Therefore it would have been prima facie obvious to one of ordinary skill in the art, at the time of filing to modify the teaching of McKay such that the two populations of particles (the bioadhesive and the penetration enhancers) were administered separately, with a reasonable expectation of success.

Since it was known in the art that the penetration enhancer and bioadhesive could be administered separately without significantly decreasing the effectiveness of the method, it would have been a matter of preference or a matter of routine optimization of the method. Regarding routine optimization, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the separate administration of the bioadhesive particles and penetration enhancers was other than routine, that the results from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-8656. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0756. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVE T. NGUYEN
PRIMARY EXAMINER

Jon Eric Angell, Ph.D.
Art Unit 1635